

| | | | | |
|---|------------------------|--|-------------------------|--|
| INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99) | Application Number | | 10616659 | |
| | Filing Date | | 2003-07-09 | |
| | First Named Inventor | | MARANAS, COSTAS D. | |
| | Art Unit | | 1631 | |
| | Examiner Name | | SKOWRONEK, KARLHEINZ R. | |
| | Attorney Docket Number | | P06367US03 (2 OF 2) | |

| U.S.PATENTS | | | | | | |
|-------------------|---------|---------------|------------------------|------------|---|--|
| Examiner Initial* | Cite No | Patent Number | Kind Code ¹ | Issue Date | Name of Patentee or Applicant of cited Document | Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear |
| | 1 | | | | | |

If you wish to add additional U.S. Patent citation information please click the Add button.

| U.S.PATENT APPLICATION PUBLICATIONS | | | | | | |
|-------------------------------------|---------|--------------------|------------------------|------------------|---|--|
| Examiner Initial* | Cite No | Publication Number | Kind Code ¹ | Publication Date | Name of Patentee or Applicant of cited Document | Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear |
| | 1 | | | | | |

If you wish to add additional U.S. Published Application citation information please click the Add button.

| FOREIGN PATENT DOCUMENTS | | | | | | | |
|--------------------------|---------|--------------------------------------|--|------------------------|------------------|---|--|
| Examiner Initial* | Cite No | Foreign Document Number ³ | Country Code ² <input type="text"/> | Kind Code ⁴ | Publication Date | Name of Patentee or Applicant of cited Document | Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear |
| | 1 | | | | | | |

If you wish to add additional Foreign Patent Document citation information please click the Add button

| NON-PATENT LITERATURE DOCUMENTS | | | | | | | |
|---------------------------------|---------|---|--|--|--|--|--|
| Examiner Initials* | Cite No | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published. | | | | | |
| | | | | | | | |

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

| | |
|------------------------|-------------------------|
| Application Number | 10616659 |
| Filing Date | 2003-07-09 |
| First Named Inventor | MARANAS, COSTAS D. |
| Art Unit | 1631 |
| Examiner Name | SKOWRONEK, KARLHEINZ R. |
| Attorney Docket Number | P06367US03 (2 OF 2) |

| | | |
|----|---|--------------------------|
| 1 | Moore et al., "Modeling DNA Mutation and Recombination for Directed Evolution Experiments" <i>J. Theor. Biol.</i> 205 (3):483-503 (2000). | <input type="checkbox"/> |
| 2 | Moore et al., "Predicting crossover generation in DNA shuffling," <i>Proc. Natl. Acad. Sci. USA</i> 98(6):3226-3231 (2001). | <input type="checkbox"/> |
| 3 | Mushegian et al., "A minimal gene set for cellular life derived by comparison of complete bacterial genomes," <i>Proc. Natl. Acad. Sci. USA</i> 93(19):10268-10273 (1996). | <input type="checkbox"/> |
| 4 | Nakamura and Whited, "Metabolic engineering for the microbial production of 1,3-propanediol," <i>Curr. Opin. Biotechnol.</i> 14(5):454-459 (2003). | <input type="checkbox"/> |
| 5 | Oh et al., "Gene expression profiling by DNA microarrays and metabolic fluxes in <i>Escherichia coli</i> ," <i>Biotechnol. Prog.</i> 16(2):278-286 (2000). | <input type="checkbox"/> |
| 6 | Overbeek et al., "WIT: integrated system for high-throughput genome sequence analysis and metabolic reconstruction," <i>Nucl. Acids. Res.</i> 28(1):123-125 (2000). | <input type="checkbox"/> |
| 7 | Palsson, "The Challenges of in Silico Biology," <i>Nat. Biotechnol.</i> 18(11):1147-1150 (2000). | <input type="checkbox"/> |
| 8 | PAPOUTSAKIS et al., "Equations and Calculations of Product Yields and Preferred Pathways for Butanediol and Mixed-Acid Fermentations", <i>Biotechnology and Bioengineering</i> 17:50-66 (1985). | <input type="checkbox"/> |
| 9 | Papoutsakis, "Equations and calculations for fermentations of butyric acid bacteria," <i>Biotechnol. Bioeng.</i> 26(2):174-187 (1984). | <input type="checkbox"/> |
| 10 | Pennisi, "Laboratory Workhorse Decoded," <i>Science</i> 277:1432-1434 (1997). | <input type="checkbox"/> |
| 11 | Pharkya et al., "Exploring the overproduction of amino acids using the bilevel optimization framework OptKnock," <i>Biotechnol. Bioeng.</i> 84(7):887-899 (2003). | <input type="checkbox"/> |

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

| | |
|------------------------|-------------------------|
| Application Number | 10616659 |
| Filing Date | 2003-07-09 |
| First Named Inventor | MARANAS, COSTAS D. |
| Art Unit | 1631 |
| Examiner Name | SKOWRONEK, KARLHEINZ R. |
| Attorney Docket Number | P06367US03 (2 OF 2) |

| | | |
|----|--|--------------------------|
| 12 | Pharka, et al., "OptStrain: A computational framework for redesign of microbial production systems", <i>Genome Res.</i> 14:2367-2376 (2004). | <input type="checkbox"/> |
| 13 | Pramanik et al., "Stoichiometric Model of Escherichia coli Metabolism: Incorporation of Growth-Rate Dependent Biomass Composition and Mechanistic Energy Requirements," <i>Biotechnol. Bioeng.</i> 56(4):398-421 (1997). | <input type="checkbox"/> |
| 14 | Quackenbush et al., "The TIGR Gene Indices: analysis of gene transcript sequences in highly sampled eukaryotic species," <i>Nucleic Acids Res.</i> 29:159-165 (2001). | <input type="checkbox"/> |
| 15 | Reed et al., "An expanded genome-scale model of Escherichia coli K-12 (iJR904 GSM/GPR)," <i>Genome Biol.</i> 4(9):R54 (2003). | <input type="checkbox"/> |
| 16 | Richmond et al., "Genome-wide expression profiling in Escherichia coli K-12," <i>Nucl. Acids Res.</i> 27(19):3821-3835 (1999). | <input type="checkbox"/> |
| 17 | SantaLucia Jr., "A unified view of polymer, dumbbell, and oligonucleotide DNA nearest-neighbor thermodynamics," <i>Proc. Natl. Acad. Sci. USA</i> , 95(4):1460-1465 (1998). | <input type="checkbox"/> |
| 18 | Savageau, "Biochemical Systems Analysis," <i>J. Theor. Biol.</i> 25:365-369 (1969). | <input type="checkbox"/> |
| 19 | Schilling et al., "The Underlying Pathway Structure of Biochemical Reaction Networks," <i>Proc. Natl. Acad. Sci. USA</i> , 95(8):4193-4198 (1998). | <input type="checkbox"/> |
| 20 | Schilling, et al, "Combining pathway analysis with flux balance analysis for the comprehensive study of metabolic systems," <i>Biotechnol. Bioeng.</i> 71(4):286-306 (2000). | <input type="checkbox"/> |
| 21 | Schilling et al., "Toward metabolic phenomics: analysis of genomic data using flux balances," <i>Biotechnol Prog.</i> 15:288-295 (1999). | <input type="checkbox"/> |
| 22 | Segre et al., "From annotated genomes to metabolic flux models and kinetic parameter fitting," <i>Omics</i> , 7(3):301-316 (2003). | <input type="checkbox"/> |

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

| | |
|------------------------|-------------------------|
| Application Number | 10616659 |
| Filing Date | 2003-07-09 |
| First Named Inventor | MARANAS, COSTAS D. |
| Art Unit | 1631 |
| Examiner Name | SKOWRONEK, KARLHEINZ R. |
| Attorney Docket Number | P06367US03 (2 OF 2) |

| | | |
|----|---|--------------------------|
| 23 | Selkov, et al., "MPW: the Metabolic Pathways Database," <i>Nucl Acids Res</i> , 26(1):43-45 (1998). | <input type="checkbox"/> |
| 24 | Sun, "Modeling DNA Shuffling," <i>Ann. Conf. Res. Comp. Mol. Biol. Proc. Second. Ann. Int'l Conf. Comp. Mol. Biol.</i> p. 251-257 (1998). | <input type="checkbox"/> |
| 25 | Supplemental European Search Report, The Penn State Research Foundation, EP 04 78 2168 dated 7-1-2009, 2 pages | <input type="checkbox"/> |
| 26 | Supplemental European Search Report, The Penn State Research Foundation, EP 0478 2168 Dated 7-8-2009. | <input type="checkbox"/> |
| 27 | TIGR-Web site. TIGR microbial database http://www.tigr.org (2009) (NOT AVAILABLE) | <input type="checkbox"/> |
| 28 | Tomita, et al., "E-CELL: software environment for whole-cell simulation," <i>Bioinformatics</i> 15(1):72-84 (1999). | <input type="checkbox"/> |
| 29 | Tomita, "The E-Cell Project: Towards Integrative Simulation of cellular Processes," <i>New Gen. Comput.</i> 18:1-12 (2000). | <input type="checkbox"/> |
| 30 | Torres et al., "An Indirect Optimization Method for Biochemical Systems: Description of Method and Application to the Maximization of the Rate of Ethanol, Glycerol, and Carbohydrate Production in <i>Saccharomyces cerevisiae</i> ," <i>Biotechnol. Bioeng.</i> 55(5):758-772 (1997). | <input type="checkbox"/> |
| 31 | Valdes et al., "Metabolic reconstruction of sulfur assimilation in the extremophile <i>Acidithiobacillus ferrooxidans</i> based on genome analysis," <i>BMC Genomics</i> 4:51 (2003). | <input type="checkbox"/> |
| 32 | VALLINO et al., "Metabolic flux distributions in <i>Corynebacterium glutamicum</i> during growth and lysine overproduction," <i>Biotechnol. Bioeng.</i> 41:633-646 (1993). | <input type="checkbox"/> |
| 33 | VARMA et al., "Metabolic Capabilities of <i>Escherichia coli</i> : I. Synthesis of Biosynthetic Precursors and Cofactors", <i>J. theor. Biol.</i> 165:477-502 (1993). | <input type="checkbox"/> |

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

| | |
|------------------------|-------------------------|
| Application Number | 10616659 |
| Filing Date | 2003-07-09 |
| First Named Inventor | MARANAS, COSTAS D. |
| Art Unit | 1631 |
| Examiner Name | SKOWRONEK, KARLHEINZ R. |
| Attorney Docket Number | P06367US03 (2 OF 2) |

| | |
|----|--|
| 34 | VARMA et al., "Stoichiometric flux balance models quantitatively predict growth and metabolic by-product secretion in wild-type <i>Escherichia coli</i> W3110," <i>Appl. Environ. Microbiol.</i> 60(10):3724-3731 (Oct 1994). <input type="checkbox"/> |
| 35 | Varmer et al., "Mathematical Models of Metabolic Pathways," <i>Curr. Opin. Biotechnol.</i> 10(2):146-150 (April 1999). <input type="checkbox"/> |
| 36 | Voit, "Optimization in Integrated Biochemical Systems," <i>Biotechnol. Bioeng.</i> 40(5):572-582 (1992). <input type="checkbox"/> |
| 37 | Wang, et al., "Cadmium removal by a new strain <i>Pseudomonas aeruginosa</i> in aerobic culture," <i>App. Environ. Microbiol.</i> 63:4075-4078 (1997). <input type="checkbox"/> |
| 38 | Xie et al., "Energy metabolism and ATP balance in animal cell cultivation using a stoichiometrically based reaction network," <i>Biotechnol. Bioeng.</i> 52(5):591-601 (1996). <input type="checkbox"/> |
| 39 | Xie et al., "Integrated approaches to the design of media and feeding strategies for fed-batch cultures of animal cells," <i>Trends Biotechnol.</i> 15(3):109-113 (1997). <input type="checkbox"/> |
| 40 | Xie et al., "Material Balance Studies on Animal Cell Metabolism Using Stoichiometrically Based Reaction Network," <i>Biotechnol. Bioeng.</i> 52:579-590 (1996). <input type="checkbox"/> |
| 41 | Xie et al., "Stoichiometric analysis of animal cell growth and its application in medium design," <i>Biotechnol. Bioeng.</i> 43 (11):1164-1174 (1994). <input type="checkbox"/> |
| 42 | Yang, et al., "Metabolic Flux Analysis of <i>Escherichia coli</i> Deficient in the Acetate Production Pathway and Expressing the <i>Bacillus subtilis</i> Acetylactate Synthase," <i>Met. Eng.</i> (1999). <input type="checkbox"/> |
| 43 | URL unix.mcs.anl.gov/otc/Guide/faq/linear-programming-faq.html , "Linear Programming Frequently asked questions," Optimization Technology Center of Northwestern University and Argonne National Laboratory (As Printed December 1, 2001). <input type="checkbox"/> |
| 44 | URL www.che.udel.edu/edwardsgroup/LAB/NBT_ExpPhPP/FBAPrimer/FBAC "Appendix 1: Flux balance analysis primer." (As printed 1/4/02) <input type="checkbox"/> |

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

| | |
|------------------------|-------------------------|
| Application Number | 10616659 |
| Filing Date | 2003-07-09 |
| First Named Inventor | MARANAS, COSTAS D. |
| Art Unit | 1631 |
| Examiner Name | SKOWRONEK, KARLHEINZ R. |
| Attorney Docket Number | P06367US03 (2 OF 2) |

| | |
|----|--|
| 45 | URL http://www.ilog.com/products/cplex/ accessed via the GAMS (Brooke, et al., (1998). <input type="checkbox"/> |
| 46 | <input type="checkbox"/> |
| 47 | <input type="checkbox"/> |
| 48 | <input type="checkbox"/> |
| 49 | <input type="checkbox"/> |
| 50 | <input type="checkbox"/> |

If you wish to add additional non-patent literature document citation information please click the Add button

EXAMINER SIGNATURE

| | |
|--------------------|-----------------|
| Examiner Signature | Date Considered |
|--------------------|-----------------|

***EXAMINER:** Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. ² Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). ³ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁴ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁵ Applicant is to place a check mark here if English language translation is attached.